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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C
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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,574	BERNER ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/29/2004, 12/5/2005, 8/7/2006, 2/12/2007 and 2/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The new examiner of record is Andriae M. Holt.

The examiner acknowledges the receipt of amendments to the specification and claims dated December 5, 2007. Claims 1-20 and 22-26 are pending in the application. Claim 21 has been cancelled.

Election/Restrictions

Applicant's election without traverse of Group A, a method of delivering an active agent, in the reply filed on December 5, 2007, is acknowledged. Applicant's election of the active agent ciprofloxacin is acknowledged.

Claims 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 5, 2007.

Claims 1-14, 18-20 and 22-26 will be examined on the merits.

Priority

This application is a divisional of U.S. Application No. 10/24,932, now abandoned, filed on December 18, 2001 which is a continuation in part of U.S. Application No. 10/045,816, now abandoned, filed on October 25, 2001.

Information Disclosure Statement

Receipt of Information Disclosure Statements filed on January 29, 2004, December 5, 2005, August 7, 2006, February 12, 2007 and February 8, 2008 is acknowledged.

Double Patenting

Claims 1, 5, and 11-13 of this application conflict with claims 17, 21 and 23 of Application No. 10/773,986. Claims 18-20 of this application conflict with claims 52 and 65-66 of Application No. 10/281,284. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, and 11-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 17, 21-23 of copending Application No. 10/773,986 (Application '986). Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed toward a method of delivering a pharmacologically active agent by orally administering to a patient in the fed mode a therapeutically effective amount of the active agent and at least one biocompatible, hydrophilic polymer that

swells upon absorption of water from gastric fluid in order to promote gastric retention. In instant claim 1, the dosage form is characterized by an erosion rate to dissolution rate ratio determined by in vitro disintegration tests and in vitro dissolution tests. Claim 17 in Application '986 claims the dosage form gradually erodes within the stomach over a determinable period of time and releases the active ingredient throughout the determined time period and that the dosage form is selected by subjecting the dosage form to a disintegration test in vitro. The instant application does not specifically recite that the dosage form will gradually erode and release the active agent throughout the determinable time period, however, it would be obvious to one skilled in the art, that if the claims possess the same active agent and biocompatible, hydrophilic polymers, they would erode within the stomach and release the active agent throughout the determinable time period. In reference to instant claims 5, 11 and 13, using the method of delivering a pharmacologically active agent wherein at least 85% of the active agent is released within six to eight hours is identical to claim 21 of Application '986. The active agent of instant claims 11 and 13 is the antibiotic ciprofloxacin, which is the same anti-microbial agent in Application '986. Therefore the scopes of the copending claims overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 18-20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 52 and 65-66 of

copending Application No. 10/281,284 (Application '284). Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed toward a method of treating a mammal by orally administering ciprofloxacin to a mammal in a fed mode once daily. The instant claims specifically state a method of treating a human patient. Application '284 uses the term "mammal". It is known in the art that a human patient is a mammal; therefore it would be obvious to treat a human with the pharmacologically active agent, ciprofloxacin once daily as claimed in Application '284. Therefore the scopes of the copending claims overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 and 22-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Shell et al. (US 5,972,389).

Shell et al. disclose a controlled-release or, alternatively, sustained-release oral drug dosage form for releasing a sparingly soluble drug into the stomach (method of

delivering a pharmacologically active agent, instant invention), the drug dosage form comprising a plurality of solid particles or pellets of a solid-state drug dispersed within a polymer (active agent, polymer, instant invention) that (i) swells unrestrained dimensionally via imbibition of gastric fluid to increase the size of the particles to promote gastric retention within the stomach of a patient in which the fed mode has been induced, (ii) gradually erodes over a time period of hours, with the erosion commencing upon contact with the gastric fluid, and (iii) releases the drug to the stomach and duodenum at a rate dependent on the erosion rate (col. 1, line s65-67-col. 2, lines 1-9) (upon imbibition of water swells, instant invention). Shell et al. disclose that polymers suitable for use in the invention have the property of swelling as a result of imbibing water from the gastric fluid, and gradually eroding over a time period of hours. Shell et al. disclose that since erosion of the polymer results from the interaction of fluid with the surface of the dosage form, erosion initiates simultaneously with the swelling process (col. 4, lines 27-34). Shell et al. further disclose that while swelling and erosion occur at the same time, the rate for achieving maximum swelling should be faster than the rate the dosage form fully erodes. Shell et al. disclose that swelling should be at a rate fast enough to allow the particles to be retained in the stomach, while erosion should be of a rate that provides the desired dosing of the drug being delivered (col. 4, lines 37-43). Shell et al. disclose in Example 4, col. 12, lines 30-51, that materials for clinical trials were prepared with a composition: 40% barium sulfate (0.01%-80% active agent, instant invention), 59.75 % polyethylene oxide (polymer, instant invention), and 0.25 % magnesium stearate. Shell et al. disclose ten normal human subjects were

administered one size 0 gelatin capsule containing the above composition. Shell et al. further disclose the subjects were in a fed mode. Shell et al. disclose the progress of the pellets through the gastrointestinal tract was monitored by X-radiology at 2,4,6,8, and 10 hours post instillation. Shell et al. disclose the results obtained support the conclusion that the oral delivery system is retained in the stomachs of human subjects for a period averaging form six to eight hours (retained in upper GI tract for 2-12 hours, instant invention). Shell et al. disclose in example 3, that the release rate of acyclovir from the table-containing capsules was found to be relatively constant up to the time of delivery of 90% of the total content, which occurs at approximately 6 hours (col. 12, lines 24-28) (at least 75% to 85 % release in time period of 2 to 12 hours or 4 to 9 hours, instant invention). Shell et al. disclose the dosage forms of the present invention are particularly useful for delivering drugs directly into the stomach for an extended period of time, for example, when the drug is preferentially absorbed there (e.g., ciprofloxacin) (col. 5, lines 7-10). Shell et al. disclose that by incorporating a drug either in a protective vesicle or enteric coating into the dosage form of the invention, the benefits of gastric retention and gradual release to the GI tract are combined with the advantageous properties of the vesicle or enteric coating (col. 6, lines 36-40). Shell et al. further disclose the advantages include protecting the drug from the detrimental environment of the GI tract (degradative enzymes a low pH). Shell et al. disclose the drug in combination with either agent is continuously and gradually released from the gastric retentive system to bathe the duodenum and small intestine in a prolonged manner which is determined by the rate at which the polymer erodes (col. 6, lines 40-49). Shell et al. further disclose less of

the drug is required to achieve therapeutic efficacy because less drug is lost as a result of degradation within the stomach (col. 6, lines 49-51) (pH, instant invention). In reference to the erosion rate to dissolution rate ratio of claims 1 and 22-24, as to the claimed properties, it would be inherent that they must be possessed by the anticipatory composition because it is the same as those claimed. Shell et al. meet all the limits of the claims.

Claims 1-3 and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al. (US 6,120,803).

Wong et al. disclose an active agent dosage form which is adapted for retention in the stomach and useful for the prolonged delivery of an active agent formulation to a fluid environment for use. Wong et al. further disclose the active dosage form is a polymer matrix that swells upon contact with the fluids of the stomach (Abstract) (active agent, polymer, swell to promote gastric retention, instant invention). Wong et al. disclose the polymer matrix will swell in the stomach and facilitate retention of the active agent reservoir in the stomach during the time that active agent is being delivered (col. 12, lines 42-44). Wong et al. further disclose that after the polymer has eroded and active agent has been dispensed, the active agent delivery reservoir will pass from the stomach and exit the gastrointestinal tract (col. 12, lines 44-48). Wong et al. disclose the active agent will be released from the dosage form at a rate that releases a therapeutically effective amount of active agent to the subject over a substantial portion of the period between administrations of the dosage forms. Wong et al. further disclose

that release will occur over 40% of the period between repeated administration of the dosage form, more preferably at least over 60% and most preferably over 80% (col. 22, lines 3-10)(at least 75%-85% over time period, instant invention). Wong et al. disclose in example 8, col. 27, lines 26-67, a gastric platform dosage form delivering the antibiotic minocylcine was fabricated. Wong et al. further disclose that four systems from the same batch of dosage forms were evaluated in vivo and that an ascending plasma concentration over a period of approximately 6 to 8 hours was observed and indicated retention of the dosage forms in the stomach and delivery of drug for a prolonged period after dosing. Wong et al. disclose the invention is useful to deliver active agents that are poorly absorbed in the lower gastrointestinal tract, but well absorbed in the upper gastrointestinal tract such as ciprofloxacin (col. 19, lines 10-24) (ciprofloxacin, instant invention). In reference to the erosion rate to dissolution rate ratio of claims 1 and 22-24, as to the claimed properties, it would be inherent that they must be possessed by the anticipatory composition because it is the same as those claimed. Wong et al. meet all the limits of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 11-14 and 18-20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Shell et al. (US 5,972,389) in view of Louie-Helm et al. Publication (2001) and Cipro® Drug Information Sheet (2000).

Applicant's Invention

Applicant claims a method of delivering a pharmacologically active agent, ciprofloxacin, orally to a patient in a fed mode. Applicant claims the method comprising combining the ciprofloxacin with at least one biocompatible, hydrophilic polymer which upon imbibition of water swells unrestrained dimensionally to a size effective to promote gastric retention. Applicant further claims a method of treating a human patient suffering from a bacterial infection once daily with ciprofloxacin.

Determination of the scope of the content of the prior art (MPEP 2141.01)

The teachings of Shell et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Shell et al. do not teach the specific active agent, ciprofloxacin, in the working examples or the method of treating a patient with a bacterial infection with ciprofloxacin as in claims 18-20. It is for this reason the Louie-Helm et al. Publication and the Cipro® Drug Information Sheet are joined.

Helm et al. teach that the pharmacokinetics of 2 formulations of gastric retentive tablets of ciprofloxacin hydrochloride and the immediate release tablet were compared in 15 healthy volunteers (Abstract). Louie-Helm et al. teach to achieve once daily administration; gastric retentive tables of ciprofloxacin hydrochloride were developed (page 1, col. 1-2, Introduction). Louie-Helm et al. teach the gastric retentive tablets are administered with food and swell to a size sufficient to be retained in the stomach in the fed mode. Louie–Helm et al. teach that to insure that ciprofloxacin would not be delivered to the colon, the period of 90% drug release in USP Type 1 dissolution testing was designed to be approximately 6 hours (page 1-2, col. 2, Experimental Methods)(claims 1-3, 11-14, and 19, delivery of ciprofloxacin, 2-12 hours, once daily, instant invention).

The Cipro ® (ciprofloxacin hydrochloride) Tablets and Cipro® (ciprofloxacin) Drug Information Sheets teach that Cipro® is a synthetic broad spectrum antimicrobial agent for oral administration (page 1, Description) (claims 11-14 and 18, ciprofloxacin, antimicrobial treatment, oral administration, instant invention). The Drug Information Sheet teaches on pages 5-6 that Cipro® is shown to be active against Pseudomonas, Shigella, Salmonella, E. coli, Campylobacter, Enterobacter and *Bacillus anthracis* (claim 20, specific bacteria, instant invention).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Shell et al., the Louie-Helm et al. Publication and the Cipro ® Drug Information Sheet to produce a method for delivering ciprofloxacin in a controlled or sustained release formulation by combining the ciprofloxacin active ingredient with a biocompatible, hydrophilic polymer that upon imbibition of water swells unrestrained to promote gastric retention. Shell et al. teach it is within the purview of one skilled in the art to provide a controlled-release or alternatively, sustained-release oral drug dosage form for releasing a sparingly soluble drug into the stomach, the drug dosage form comprising a plurality of solid particles or pellets of a solid-state drug dispersed within a polymer that swells unrestrained dimensionally via imbibition of gastric fluid to increase the size of the particles to promote gastric retention within the stomach of a patient in which the fed mode has been induced, that gradually erodes over a time period of hours, with the erosion commencing upon contact with the gastric fluid and that releases the drug to the stomach and duodenum at a rate dependent on

the erosion rate. Shell et al. also teach that the dosage forms are useful for delivering drugs directly into the stomach for an extended period of time when the drug is preferentially absorbed there using the example of ciprofloxacin. The Louie-Helm et al. Publication teaches it is within the purview of one skilled in the art to study the pharmacokinetics of a once daily gastric retentive ciprofloxacin hydrochloride tablet that was administered to patients and the Cipro ® Drug Information Sheet teaches the indications for the use of ciprofloxacin hydrochloride and ciprofloxacin. One skilled in the art at the time of invention would have been motivated to combine the teachings of the three references to produce a method of delivering a pharmacologically active agent, ciprofloxacin, that has gastric retentive properties as Shell et al. teach ciprofloxacin is a good candidate for an active agent to be used in the dosage form because it is readily absorbed in the stomach and ciprofloxacin is used to effectively treat bacterial infections. Given the state of the prior art as evidenced by the teachings of the cited references, and absent any evidence to the contrary, there would have been a reasonable expectation of success in combining the cited references to produce a method of delivering a ciprofloxacin active agent that has gastric retentive properties to treat a patient that has a bacterial infection. The gastric retentive ciprofloxacin would have the benefit of a reduction in side effects from the drug and an ability to effect treatment with less frequent administration of the drug being used.

None of the claims are allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 9:00 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616